

that she had reviewed the previous submission of WO 96/34888, filed with the Supplemental Amendment C After Final, and on the basis of that review was withdrawing the §112, first paragraph rejection based on "lack of enablement."

New claims 44-47 are now pending in this application. Claim 44 is directed to a method in which an inoculum, comprising a vehicle containing a cholesteryl ester transfer protein (CETP) immunogen, is administered to a human in order to produce antibodies which bind to cholesteryl ester transfer protein (CETP) in the blood of the human patient. The CETP immunogen has (i) an exogenous antigenic carrier polypeptide that is peptide-bonded to (ii) an immunogenic polypeptide comprising amino acids 465 through 475 of human CETP amino acid sequence (SEQ ID NO: 28). According to the claim, administration of the immunogen is repeated at an interval of about three to six months to cause an autogeneic immunological response and to maintain the antibodies by further administration of the inoculum at an interval of about 9 to 18 months. The object of this therapy is to lessen the transfer of cholesteryl ester from HDL and increases the concentration of HDL cholesterol in the blood of the human patient.

Presented immediately below is a claim chart identifying specific support in the pending application for the subject matter of claim 44.

Claim Language	Specification Support
A process for producing antibodies to cholesteryl ester transfer protein (CETP) in the blood of a human whose blood contains CETP, said process comprising the steps of:	" A contemplated process is useful in treating human pro-atherogenic dyslipoproteinemias characterized by low HDL/LDL cholesterol ratios." Page 8, ln 33-35. "The present invention relates to a process for increasing the ratio of HDL cholesterol to LDL cholesterol in the blood of a treated mammal that has CETP in its blood, and that in humans leads to an amelioration of dyslipoproteinemias characterized by low HDL/LDL cholesterol ratios." Page 13, ln 12-17.

<p>(a) administering an inoculum to said human, said inoculum comprising a vehicle containing a CETP immunogen,</p>	<p>“[I]mmunizing the mammal to be treated with an inoculum containing a CETP immunogen that is dissolved or dispersed in a vehicle.” Page 9, ln. 7-9.</p> <p>“The CETP immunogen comprises an immunogenic polypeptide having a CETP amino acid residue sequence that is covalently bonded to an exogenous antigenic polypeptide carrier.” Page 9, ln 9-12.</p> <p>“A CETP immunogen is dissolved or dispersed in a pharmaceutically acceptable vehicle composition that is preferably aqueous to form an inoculum...” Page 25, ln. 22-24.</p> <p>Page 26, ln. 5-12.</p>
<p>wherein said CETP immunogen has (i) an exogenous antigenic carrier polypeptide that is peptide-bonded to (ii) an immunogenic polypeptide comprising amino acids 465 through 475 of human CETP amino acid sequence (SEQ ID NO: 28);</p>	<p>“[T]he immunogenic polypeptide is a portion of a CETP molecule that is covalently bonded to an exogenous antigenic carrier.” Page 9, ln. 23-25</p> <p>“It is preferred that the covalent bond used to link the exogenous antigenic carrier and immunogenic polypeptide be a peptide bond.” Page 16, ln. 6-8</p> <p>“fusion protein” Page 9, ln. 28 and page 16, ln 11.</p> <p>“The term ‘fusion protein’ is used to denote the expression product of two or more different genes in which the amino acid residue sequences of both genes are expressed peptide-bonded together as a single molecule.” Page 11, ln. 24-27.</p> <p>“A particularly preferred polypeptide immunogen has an amino acid residue sequence that includes positions 465 through 475 of human CETP or an analogous position of CETP from another source...” Page 23, ln 1-4.</p>

<p>(b) repeating said administration at an interval of about three to six months, sufficient for said CETP immunogen to cause, by an autogeneic immunological response, production of antibodies which bind to CETP in the blood of said human and</p>	<p>"The present invention contemplates an autogeneic immunological process for lessening the transfer of cholestryl esters from HDL particles and for increasing the HDL cholesterol concentration of a mammal whose blood also contains CETP." Page 8, ln 29-33.</p> <p>"[I]t utilizes the host mammal's own (autogeneic) immunological system to provide a desired result, thereby obviating problems associated with repeated administration of xenogeneic antibodies that themselves become immunogenic in the host animal." Page 10, ln. 17-21.</p> <p>"The term 'CETP immunogen' is used to denote [a] molecule that is used to induce the production of antibodies that immunoreact with (bind to) CETP." Page 11, ln. 15-17.</p> <p>See also, page 13, ln. 27 to Page 14, ln. 6.</p> <p>"A CETP immunogen . . . when administered to a mammal whose blood contains CETP in an effective amount, induces the production of antibodies that immunoreact with (bind to) CETP and lessen the transfer of cholestryl esters from HDL particles" Page 25, ln. 22-28.</p> <p>"It is particularly contemplated once the desired antibodies are induced in the mammal that the immunization step be repeated at intervals of about 3 to about 6 months..." Page 29, ln. 16-19.</p>
<p>(c) maintaining said antibodies which bind to CETP in the blood of said human by further administration of said inoculum at an interval of about 9 to 18 months,</p>	<p>"The production of antibodies that bind to CETP is readily ascertained by obtaining a plasma or serum sample from the immunized mammal and assaying the antibodies therein for their ability to bind CETP as an antigen in an ELISA assay as described herinafter or by another immunoassay such as a Western blot as is well known in the art." Page 27, ln. 30-34, page 28, ln. 1-2.</p> <p>"The mammal is thereafter preferably</p>

	maintained at that increased HDL cholesterol level by periodic booster immunizations administered at intervals of about 9 to about 18 months. Page 29, ln. 24-27.
whereby the binding of said antibodies to CETP in said blood lessens the transfer of cholestryl ester from HDL and increases the concentration of HDL cholesterol in the blood of said human.	"That desired raising of the HDL/LDL cholestrerol ratio is accomplished immunologically by antibodies induced in the blood of the treated mammal that recognize circulating CETP." Page 13, ln. 17-20. "...a process for lessening the transfer of cholestryl esters from HDL particles and increasing the concentration of HDL cholesterol in the blood of a mammal whose blood contains cholesterol ester transfer protein (CETP)." Page 14, ln. 18-22.

Support for new claim 45 is found in Example 3 and specifically in subpart C. See particularly the discussion surrounding line 35 of page 44.

Support for new claims 46 and 47 is found on page 16, lines 15-18 and on page 18, lines 11-19.

On the basis of the above, applicants submit the pending claims for examination. Applicants respectfully request consideration of the subject application.

Respectfully submitted,

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